be shortened if the solubility of haemoglobin is reduced so that cells become more rigid than normal and cannot pass easily through the microvasculature. This is the basis of the mild haemolytic anaemia seen in the haemoglobin-C disorders.[14] Finally, a whole series substitutions may alter the stability of the haemoglobin molecule. These conditions form the clinical syndrome of the unstable-haemoglobin disorders.[15 16] Affected patients have a variable haemolytic anaemia with inclusion bodies in their red cells which result from instability of the affected haemoglobin molecules and their precipitation in the cell. In addition they may pass dark urine owing to the production of haem-breakdown products (dipyrolles) from the precipitated haemoglobin. The different types of substitution which can produce this clinical picture are summarized in the table.

Single amino-acid substitutions may also alter the function of haemoglobin. In some cases replacements near the haem pocket result in permanent methaemoglobin formation. There are a series of haemoglobins, all designated "M" followed by their place of discovery—for example Hb M Boston, M Saskatoon, which are associated with permanent cyanosis.[17] In addition there is a steadily growing group of variants which are associated with hereditary polycythaemia.[18 19] In these cases the amino-acid substitution results in an abnormal oxygen-dissociation curve and a high oxygen-affinity state such that the red cells give up relatively less oxygen in the tissues, which results in increased erythropoietin production and in an increased red-cell mass.

OTHER TYPES OF MUTATION CAUSING STRUCTURAL HAEMOGLOBIN VARIANTS

Some unstable haemoglobin variants result from a deletion (loss) of one or several amino-acids in a globin chain. The molecular mechanism for this unusual condition is probably chromosomal misalignment during meiosis with the loss of one or more base triplets due to abnormal crossing over. Usually the deletion results in an unstable molecule and hence in congenital inclusion-body anaemia.[16] Other forms of genetic accidents can occur during meiosis. Unequal crossing over may cause additional genetic material to be inserted into a haemoglobin gene.[20 21] If this caused lengthening of a globin chain at a critical area it could cause an unstable-haemoglobin disorder. In some cases fusion genes are formed, such as the δβ fusion gene which leads to the production of Hb Lepore, a variant with normal α-chains combined with non-α-chains made up of the N-terminal residues of the δ-chain fused to the C-terminal residues of the β-chain.[22] The composite δβ-chain is synthesized slowly and results in the clinical picture of thalassaemia. Indeed the Hb-Lepore abnormality was the first form of thalassaemia to be worked out at the molecular level. At least four fusion haemoglobin variants are now fully characterized. The latest, Hb Kenya, has non-α-chains which consist of part γ- and part β-chain sequences—that is, a composite fetal/adult globin chain.[23 24]

The concluding part of this lecture will appear in next week's issue.

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Imported Diseases

Undiagnosed Fever—Rickettsial, Viral, and Helminth Infections

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Rickettsial Infections

TYPHUS FEVER

Typhus fever is rarely imported into the United Kingdom. A recent traveller from Bangladesh developed headache, rigors, and fever six days after arriving in England. A provisional diagnosis of malaria was excluded by examination of blood films and treatment was started with co-trimoxazole for suspected typhoid fever but without response. Cultures for *S. typhi* and the Widal reaction were negative. Re-examination of the patient showed an "eschar" on his back, and the Weil-Felix reaction subsequently confirmed the diagnosis of scrub typhus. This infection has an incubation period of 4-10 days and is characterized by headache, persistent fever, lymphadenopathy, splenomegaly, and a maculopapular rash. The eschar, which appears as a scab or ulcer, indicates the site of inoculation and multiplication of the infecting organism of scrub typhus, *Rickettsia orientalis*.

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Imported Diseases, their Incubation Periods, and where they occur

Incubation Period	Disease	Areas in Which Disease is Endemic
Short (up to 10 days)	Scrub Typhus	N. India, Pakistan, South-East Asia, N.E. Australasia, and Queensland
	Dengue Fever	Tropical and sub-tropical countries
	Yellow Fever	Africa, Central and South America
Intermediate (up to 21 days)	Malaria (can be longer)	Tropical and sub-tropical countries
	Typhoid Fever	Tropical and sub-tropical countries. Mediterranean littoral
	African Trypanosomiasis	Africa (between 12°N and 25°S)
	Schistosomiasis (can be up to 4 weeks) { Haematobium	Nile Valley, Africa, Iraq, Bombay area of India
	Schistosomiasis (can be up to 4 weeks) { Mansoni	Nile Valley, Africa, Arabia, Central and South America
	Smallpox	India, Pakistan, Bangladesh, Ethiopia, Nepal
	Brucellosis	World-wide
	Lassa Fever	West Africa
Long (over 21 days)	Kala-Azar	N., E. and W. Africa, Arabia, E. India, China, South America
	Viral Hepatitis (2-6 weeks)	World-wide, but especially in tropical and sub-tropical countries
	Filariasis	Africa, South-East Asia, N. Australia, West Indies, South America
	Hepatic Amoebiasis	Tropical and sub-tropical countries

Other rickettsial infections include epidemic and endemic typhus, Rocky Mountain spotted fever and other forms of tick typhus, and Q fever. The typhus fevers respond to chloramphenicol.

Viral Infections

SMALLPOX

The early stage of smallpox is characterized by high fever associated with non-specific symptoms, particularly headache and pain in the back. There may be a transient maculopapular rash during the prodromal illness. The incubation period is usually 12 days but may be longer. Attacks modified by previous vaccination lead to diagnostic difficulty, particularly as the classical vesicular skin eruption may not develop. The possibility of smallpox should be considered in every patient with unexplained fever who has recently visited the five countries of the world where this disease is still endemic—namely, India, Pakistan, Bangladesh, Nepal and Ethiopia. The likelihood of smallpox re-appearing in countries other than these five should always be remembered.

LASSA FEVER

This recently recognized infection was first reported from Lassa in Nigeria in 1969. The incubation period may vary from 3 to 21 days. The cause is a virus which is considered to be a member of a new group of agents named the arenoviruses. The disease presents insidiously with fever, nausea, headache, and backache. There may also be chest pain, bleeding into skin and mucous membranes, and low blood pressure. Sore throat with an adherent tonsillar exudate may develop. Diagnosis depends on the detection of serum antibodies several weeks after the onset of fever; hence early confirmation of diagnosis is impossible.

VIRAL HEPATITIS

Infectious hepatitis, which has an incubation period of two to six weeks, is widespread throughout tropical and sub-tropical countries. The prodromal illness may present with fever and non-specific symptoms but the diagnosis usually becomes obvious as jaundice develops. Viral hepatitis in Asian patients is quite commonly associated with the presence of Hepatitis-Associated (Australia) Antigen in the blood. This should be looked for in all patients developing jaundice after returning from tropical and sub-tropical countries.

DENGUE FEVER

This arbovirus infection has an incubation period of four to six days. The onset is variable but it may present with fever, headache, and aching in the joints. The disease occurs in many tropical and sub-tropical countries and is not normally fatal. The pulse rate is often relatively slow compared with the height of fever and there is also leucopenia. A maculopapular rash may develop after an afebrile period of one to two days, which usually occurs after the initial illness. The diagnosis is confirmed retrospectively by serum antibody studies.

YELLOW FEVER

Yellow fever is also an arbovirus infection and is transmitted to man by the bite of a mosquito. It is endemic in Western and Central Africa and also in the Middle East, Rhodesia, and Central and South America. The incubation period is from three to seven days. The illness frequently starts with fever and leucopenia but the subsequent course is variable. The patient usually has severe headache, aching in the limbs, and conjunctival injection. There may be persistent vomiting with abdominal pain. Bradycardia develops as the disease progresses and the patient becomes jaundiced with a haemorrhagic tendency. Death may occur rapidly in some patients. The diagnosis is confirmed by serum antibody studies.

Helminth Infections

FILARIASIS

Wuchereria bancrofti filariasis has an incubation period of at least three months and is widespread throughout tropical Africa, South-East Asia, and South America. The first manifestations of the infestation are usually attacks of fever accompanied by pain and tenderness along the course of inflamed lymphatics. The initial illness normally settles spontaneously but febrile attacks recur. After many years lymphatic obstruction eventually leads to thickening of the skin and subcutaneous oedema—hence the name "elephantiasis." In the early stages the diagnosis of filariasis may be difficult. There is usually an eosinophilia and after several months microfilariae may be seen in blood taken at night. There is a complement fixation test which is positive in a number of cases. Treatment requires specialized knowledge.

SCHISTOSOMIASIS (BILHARZIASIS)

Schistosomiasis follows penetration of the skin by the cercarial stage of the fluke which has developed in a fresh-water snail. After the initial invasion of the skin, which may be accompanied by itching, there is a symptom-free period of three to four weeks. Allergic manifestations of the disease then develop producing fever, headache, cough, and enlargement of the spleen. These slowly subside and the subsequent course of the illness depends on the type of infection. *Schistosoma mansoni*, which is highly endemic in the Nile Valley and also occurs in other parts of Africa, Arabia, and Central and South America, infects the

gastrointestinal and hepatobiliary tracts. *S. haematobium*, which principally infects the renal tract, is similarly highly endemic in the Nile Valley but is also found throughout Africa and Arabia, in Iraq and Iran, and in a small area of India around Bombay. During the initial febrile illness eosinophilia occurs but it is frequently impossible to make a definitive diagnosis of schistosomiasis at this stage. During the later stages of the disease, however, the characteristic eggs can be seen on microscopy of stool or urine. There is also a fluorescent antibody test. Treatment requires experience of the disease.

General Practice Observed

Communications between General Practitioners and Consultants

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Summary

During 1972-3 a survey was made of the pattern of communication between 80 consultants in four hospitals in south-east England and 100 general practitioners in the catchment areas of these hospitals. This aimed to identify the factors which affect the efficiency of communication between these two groups and to look for ways of improving this.

Face to face contact between consultants and general practitioners was extremely limited. The main communication links were the letters of referral and discharge, but even this form of communication had serious defects. Though most doctors were satisfied with communications in general the evidence suggested ways of improving communication between consultants and general practitioners, such as encouraging domiciliary visits where both doctors are present and consultant sessions in health centres, but that any innovation in this field could only be successful if the attitude of the consultants and general practitioners were in harmony with the new venture.

Introduction

The Harvard Davis Report states that the primary object of all medical care "is to meet the health needs of the individual and the society in which he or she lives; medicine must be integrated with other skills and disciplines and there must be a balance between care within and care outside the hospital,"[1] and the Gillie Report had earlier stated, "It has been estimated that in this country some 90% of all medical episodes are handled from start to finish by the family doctor. . . . The admission of a patient to hospital often represents only a brief, but very expensive episode in the long-term care of an individual by his general practitioner."[2] Hence close co-operation between hospital and general practice is a prerequisite of satisfactory medical care, but does this exist? The Porritt Report[3] suggests that it does not:

"The various branches of the medical profession are isolated as regards co-ordination, planning, and development of their services. The general practitioner, though accepted as the key figure in the Health Service, is isolated both administratively and clinically from the hospital and the local health authority. What exists is an artificial tripartite division of the present National Health Service organization."

The reorganization of the Health Service is intended to break down these barriers but it is doubtful, because of the lack of factual information, if the profundity of these divisions and the factors underlying them are fully appreciated.

"The British medical system is based on the principle of referral and this is likely to continue."[4] It is claimed that communication between consultant and general practitioners has become almost solely dependent on the letter of referral and reply, a type of two-way exchange of facts and opinions which implies mutual isolation.[5,6] Almost every report on the National Health Service since its inception has made some sort of recommendation about the general practitioner playing a bigger part in the hospital service.[1,2,7] Very few beds, however, are available to general practitioners in consultant-orientated hospitals,[8] and only a few specialist departments in any particular hospital provide openings for clinical assistants, mainly in casualty work and anaesthetics.[9-11] The evidence indicates that bringing together these two sections of the Health Service will be a formidable task.

Our aims in this study were: (*a*) to look at communication patterns between the consultants and general practitioners to identify the factors which influence their efficiency; (*b*) to find out what doctors' attitudes are to present forms of communication between the hospital and general practitioner service; and (*c*) to look for ways in which communications, and thus mutual relations, might be improved between consultants and general practitioners to the benefit of the communities they serve.

Method

Four acute general hospitals and their catchment areas were selected for the study, on the basis of information provided by the North East Metropolitan Regional Hospital Board (table I).[12] Two hospitals were large by regional standards and two were small. Environmentally, both A hospitals were similar in so far as the populations in their catchment areas were relatively

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